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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/117,246	12/03/1998	DOLORES LUDEVID	50062/004001	3466

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BOSTON, MA 02110

EXAMINER

KALLIS, RUSSELL

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 12/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/117,246

Applicant(s)

LUDEVID ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 42-83 is/are pending in the application.
- 4a) Of the above claim(s) 51,56,65-68 and 76 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 64 is/are allowed.
- 6) ☒ Claim(s) 42,43,45-50,52-55,57-63,69-75 and 77-83 is/are rejected.
- 7) ☒ Claim(s) 44 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

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DETAILED ACTION

Claims 1-41 are cancelled. Claims 42-83 are pending. Claims 51, 56, 65-68 and 76 are withdrawn. Claims 42-50, 52-55, 57-64, 69-75, 77-83 are examined.

Rejection of Claims 1, 3, 42 and 44 under 35 U.S.C. 102(b) is withdrawn in view of Applicant's amendments.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth: Claims 55 and 62 recite sequences shown in Figures 9, 10 or 11.

§ 1.821 Nucleotide and/or amino acid sequence disclosures in patent applications;

(d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Applicant must amend the claims, specification, and/or drawings to insert sequence identifiers.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 47-50, 52-55, 57-63, 69-75 and 77-83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection. The added claimed material which is not supported by the original disclosure is as follows: Claim 47 has been amended to recite "proline-type". There is no support in the specification or the originally filed claims for "proline-type". Applicant is invited to point to the page and line number in the specification where support can be found. Absent of such support, Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 47-50, 52-54, 57-61, 63, 69-75 and 77-82 remain and new Claim 83 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official action mailed 4/20/2004. Applicant's arguments filed 9/23/2004 have been considered but are not deemed persuasive.

Applicant asserts while they do not agree with the Office's basis for the written description rejection (i.e. failure to describe structural features common to members of the claimed genus of polynucleotides encoding plant reserve proteins having P-K concatenations), they have amended Claim 47 to recite "having in its primary structure, tandem repeats which are rich in proline-type amino acid residues" and that the rejection should be withdrawn (response page 10). Applicants have not described a representative number of sequences encoding a plant

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protein reserve comprising "tandem repeats rich in proline-type amino acid residues" other than the polynucleotides encoding a modified 28kDa gamma zein protein reserve from maize comprising high lysine modifications as P20γZ (SEQ ID NO: 11) having K-(P-K)₄ (SEQ ID NO: 3) inserted after the Pto-X domain; H30γZ (SEQ ID NO: 7) having K-(P-K)₄ (SEQ ID NO: 3) replacing the Pro-X domain; H45γZ (SEQ ID NO: 9) having K-(P-K)₄-E-F-K-(P-K)₄ (SEQ ID NO: 4) replacing the Pro-X domain; and pN13γZ having SEQ ID NO: 5 inserted 5 amino acid residues upstream of the carboxy terminus of the 28kDa gamma zein peptide (see Figure 3). Further, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides encoding plant reserve proteins, other than the tandem repeats which are rich in proline-type amino acid residues see nucleotides 91-236 of figure 9 (i.e. SEQ ID NO: 6).

Claims 47-50, 52-54, 57-61, 63, 69-75 and 77-82 remain and new Claim 83 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Maize transformed with SEQ ID NO: 6, 8, or 10, does not reasonably provide enablement for any plant transformed and stably expressing any plant reserve protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official action mailed 4/20/2004. Applicant's arguments filed 9/23/2004 have been considered but are not deemed persuasive.

Applicant asserts that the claims contain sufficient features supported by the specification to obtain the sequences, cells, and plants of the invention (response last two lines of page 11). The claims are broadly drawn to polynucleotides encoding plant reserve proteins having in its primary structure, tandem repeats which are rich in proline-type amino acid residues as

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candidates for lysine enrichment, the only support in the specification for polynucleotides encoding plant reserve proteins having in its primary structure, "tandem repeats which are rich in proline-type amino acid residues" is for the 26 kDa gamma zein protein from maize in figure 9, see amino acids encoded within nucleotides 91-236).

Applicant asserts that the skilled artisan has basic knowledge that would enable the insertion of a foreign sequence into a site of a protein to permit correct expression and localization and that the testing of recombinant constructs comprising said sequences would not require undue experimentation (response pages 12 and 13), and that the amount of guidance presented and the presence of working examples fully enable the invention as broadly claimed (response page 14). The unpredictability in an attempt to stably express a modified plant protein reserve comprising a tandem repeat rich in proline-type amino acids comprising an oligonucleotide encoding (P-K) repeats is illustrated in an example where introduction into *Arabidopsis* of a polynucleotide encoding a 28kDa gamma zein reserve protein modified to have K-(P-K)₄ (SEQ ID NO: 3) inserted after the Pto-X domain i.e. P20γZ (SEQ ID NO: 11) and to have K-(P-K)₄ (SEQ ID NO: 3) replacing the Pro-X domain i.e. H30γZ (SEQ ID NO: 7) by the inventors, resulted in premature degradation in the transformed seeds (Alvarez I. *et al.* Planta, 1998, Vol. 205; pages 420-427; see page 421, column 1, lines 42-48; and page 424, column 2 2nd paragraph lines 5-6). Applicant only teaches increased lysine content in maize endosperm transformed with polynucleotides encoding 28kDa gamma zein from maize comprising modifications as P20γZ (SEQ ID NO: 11) having K-(P-K)₄ (SEQ ID NO: 3) inserted after the Pto-X domain; H30γZ (SEQ ID NO: 7) having K-(P-K)₄ (SEQ ID NO: 3) replacing the Pro-X domain; and H45γZ (SEQ ID NO: 9) having K-(P-K)₄-E-F-K-(P-K)₄ (SEQ ID NO: 4) replacing

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the Pro-X domain (see specification pages 27-28 and Figure 3). See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a “mere germ of an idea does not constitute [an] enabling disclosure”, and that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention.

Given the unpredictability in the art for making or using DNA sequences encoding modified plant reserve proteins, comprising proline tandem rich repeats of unspecified length, number and identity, comprising any number of P-K concatenations that would stably express in a transformed plant; the breadth of the claims encompassing any plant transformed therewith; the lack of guidance in the examples of the specification or in the prior art as to which reserve proteins having proline rich tandem repeats, would when modified for high lysine express a stable protein in any host plant; and the undue trial and error experimentation required to practice the claimed invention, the invention is not enabled for the scope set forth in the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47-50, 52-55, 57-63, 69-75 and 77-83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 47, line 3, recites “proline-type”. It is unclear what are the metes and bounds of a “proline-type” residue.

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 42-43 and 45-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Gaisser, S. Molecular Microbiology 1991, Vol. 5, No. 11; pages 2777-2787; submitted as GenBank Accession Number S80675. The reference teaches $K-[P-K]_n$ where $n=5$, and thus the reference teaches all the limitations of Claims 42-43 and 45-46. Amending the rejected claims to replace “comprising” with either --having-- or --consisting of-- would obviate this rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Claims 44, 47-50, 52-55, 57-64, 69-75 and 77-83 are deemed free of the prior art given the failure of the prior art to teach or reasonably suggest plants transformed with polynucleotides encoding modified reserve proteins comprising concatenations of P-K and expressing said proteins in a stable and functional manner.

Claims 42-43, 45-50, 52-55, 57-63, 69-75 and 77-83 are rejected.

Claim 44 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 64 is allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
December 1, 2004

DAVID H. KRUSE, PH.D.
PATENT EXAMINER
